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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 09/908,994
Filing Date: July 17, 2001
Appellant(s): SHIGEURA ET AL.

Eli A. Loots, Reg. No. 54,715
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 20 November 2007 appealing from the Office action mailed 25 May 2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

5,593,838	ZANZUCCHI et al.	1-1997
5,607,646	OKANO et al.	3-1997
5,962,228	BRENNER	10-1999

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,593,838 (Zanzucchi et al.) in view of US Patent 5,607,646 (Okano et al.) and US Patent 5,962,228 (Brenner).

For convenience, claim 21, the sole independent claim, is reproduced below.

21. A method for isolating one or more different-sequence polynucleotides from a mixture, the method comprising:

(a) flowing the mixture through a flow path containing a plurality of solid supports which are located in series in the flow path, such that the mixture flows serially through each of the plurality of solid supports, each support having bound thereto a sequence-specific capture agent complementary to a different-sequence polynucleotide, under conditions effective to specifically bind different-sequence polynucleotides to corresponding sequence-specific capture agents on one or more of the supports,

(b) after step (a), releasing bound polynucleotides from a selected support by altering a physical property of that support while leaving unaltered the same physical property of at least one other of the supports, wherein the physical property is temperature, and wherein said releasing is accomplished by heating a first solid support; and

(c) eluting the released polynucleotides through the flow path such that the eluted polynucleotides can be isolated in separated form.

For purposes of examination claim 21 has been interpreted as encompassing the isolation of from one to an infinite number of nucleic acid sequences, and that at a minimum, two different capture moieties are to be present and are bound at two different locations on a support that can virtually be of any shape but can act as a flow path for a mixture of nucleic acids capable of flowing.

Zanzucchi et al., disclose a method of isolating one or more different-sequence polynucleotides from a mixture. At column 2, bridging to column 3, Zanzucchi et al., disclose using an array of wells in serial fluid connection, through which a sample is caused to pass.

Zanzucchi et al., column 5, fourth paragraph, teaches that the device may comprise thin film transistors so to provide power to the wells via leads and electrodes.

Zanzucchi et al., column 8, teaches that beads can be placed in one or more of the wells, and that the beads can have bound to their surface DNA material, e.g., probe or capture sequences.

Zanzucchi et al., column 2, teach explicitly of using the device to generate PCR fragments that can be subject to an assay/analysis. At column 9, first paragraph, Zanzucchi et al., speak explicitly of having incorporated heating and cooling means in the well as well as the use of pumping means to move a sample from one well to another. At column 10, Zanzucchi et al., speak of conducting PCR wherein the primer is immobilized to a solid support. Such a teaching speaks directly to the presence of a heating/cooling means for the second well, else, strand dissociation and reannealing would not be able to take place.

Zanzucchi et al., column 10, fourth paragraph, teach that all of the wells in each module are connected together via one or more channels. Accordingly, one can cause the sample mixture to flow in a serial manner through each of the plurality of solid supports.

Zanzucchi et al., column 10, teaches that the probes may be synthesized directly into a well.

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Zanzucchi et al., column 8, fourth paragraph, teaches explicitly that “[a]dditional devices can be built into the wells.” Such a showing clearly speaks to the further adaptation of the device so to accommodate any structure and arrangement the ordinary artisan desires.

Okano et al., column 2, second and fifth paragraphs, teaches:

It is an objective of the present invention to provide a polynucleotide capturing chip capable of simultaneously capturing a plurality of target polynucleotides, to provide a method for detecting a plurality of polynucleotides using the same and to provide a method for separating a plurality of target polynucleotides

[E]ach cell of the polynucleotide capturing chip to be used as the polynucleotide capturing support also functions as an electrode for eluting the target polynucleotides, wherein the electric fields applied to such electrodes each with a plurality of immobilized probes can be switched over one by one to elute and separate a plurality of the target polynucleotides.

Okano et al., third column, bridging to column 4, teaches that the combination of heating and reversal of electric field can be used to achieve elution of specifically captured sequences from specific wells/regions of the chip, while retaining the captured polynucleotide bound at other positions.

While Okano et al., uses a single substrate, it has been fashioned into a series of cells, and the temperature and electric field of each is under control, thereby allowing for individual, serial, or simultaneous elution of released polynucleotides.

Brenner, column 15, teaches that an array can be fashioned from a plurality of microparticles that are brought into contact with a support. And that the microparticles may comprise tag complements.

In view of the teachings of the prior art of record, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have combined the microparticles

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of Brenner in the individual cells of the array of Okano et al., with the series of wells/array of Zanzucchi et al., whereby the device would be used in a polynucleotide assay whereby specific binding reactions can take place at selected supports and eluted from same, and that the mixture would flow in a serial fashion through each of the solid supports. In view of the well-developed state of the art, said ordinary artisan would have had a most reasonable expectation of success. Therefore, and in the absence of convincing evidence to the contrary, claims 21-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,593,838 (Zanzucchi et al.) in view of US Patent 5,607,646 (Okano et al.) and US Patent 5,962,228 (Brenner).

(10) Response to Argument

At page 10, lines 4-5, of the Brief, agreement is reached that “one embodiment of Zanzucchi discloses using an array of wells in serial fluid connection.”

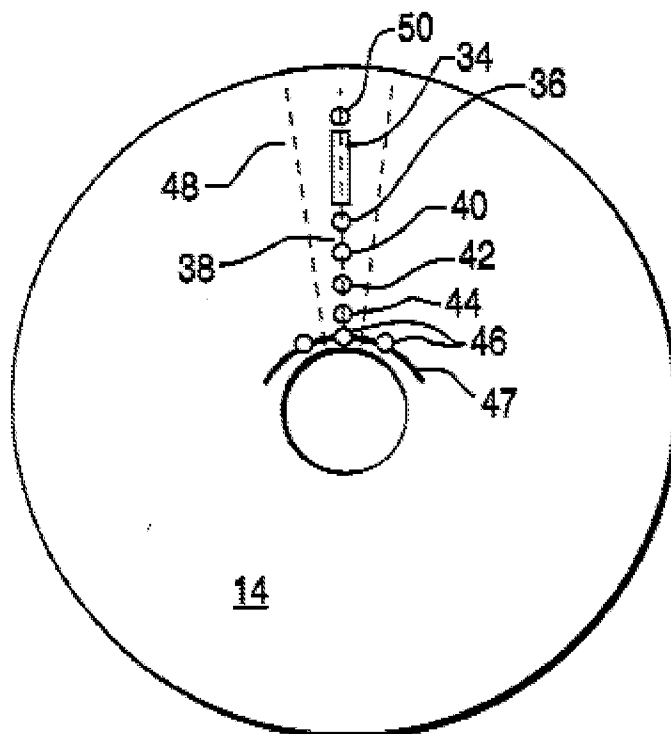
At page 10, bridging to page 11 of the Brief, argument is presented that the claimed invention requires the serial flow of a mixture through each of a plurality of supports before one releases bound polynucleotides from selected supports and that the method of Zanzucchi et al., disclose a step-wise method of treating a sample. At page 11, appellant asserts: “Zanzucchi’s stepwise approach is very different from the claimed method, in which the initial mixture is flowed through a plurality of solid supports prior to altering a physical property of any given support.” (Emphasis in the original.)

The above argument has been fully considered and has not been found persuasive. Zanzucchi et al., teach a variety of methods by which the claimed invention can be used. As seen therein, the device can be used not only for detecting a single target via specific binding in a

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single well, but also disclose having a plurality of binding agents in "successive wells" (column 11). While the aspect of placing a specific binding member in successive wells is directed to the use of antibodies, it would have been obvious to have included a plurality of nucleic acid probes in successive wells, as the benefit of multiple specific binding members would have increased the applicability, usefulness and sensitivity of the assay while reducing associated cost. Further, said ordinary artisan would have been motivated to have included a plurality of nucleic acid binding members as Okano et al., teaches using virtually any number of probes.

Zanzucchi et al., column 6, teaches that "module 48 illustrated in FIG. 1B comprises four connecting wells, but this is by way of example only, and more or fewer wells can be present depending on the tests or synthesis to be performed in each module."

**FIG. 1B**

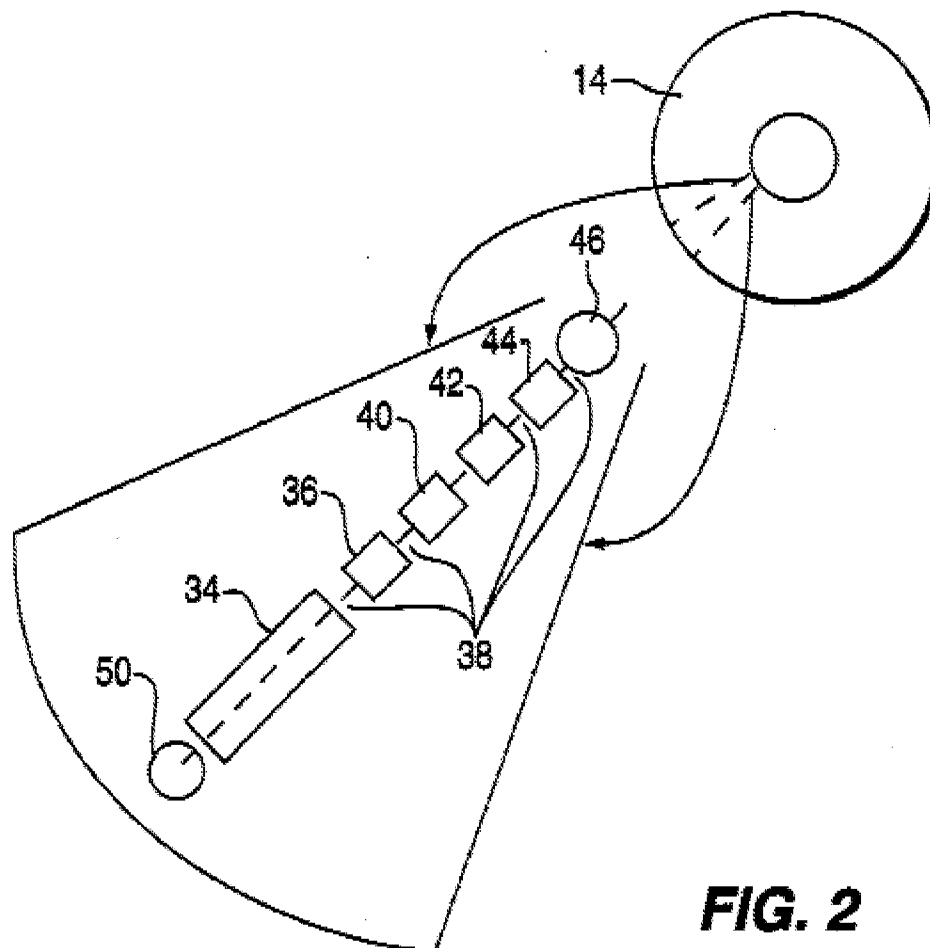


FIG. 2

Zanzucchi et al., column 7, penultimate paragraph, teaches: “In the case where the temperature of a particular well is to be monitored or changed, a means for heating or cooling the well is built into the well...”

The aspect of Zanzucchi et al., disclosing means to seal a well during heating (column 9) does not teach away from the claimed method. It is noted that the method disclosed at column 9 of Zanzucchi et al., has the fluid heated to 100 C and that such was done to inactivate proteinase K. Such are not limitations of the claimed method. Indeed, the claimed method only requires that there be some heating. No requirement is made as to how what temperature or for how long heating is to be carried out. Further, Zanzucchi et al., does not depict any sealing member

between wells in FIG. 1B, nor does Zanzucchi et al., teach that said sealing member must be used in combination with heating means. As noted above, Zanzucchi et al., teaches a plethora of embodiments, which can be mixed and matched to the ordinary artisan's wishes or requirements.

At page 11, last paragraph, of the Brief appellant asserts that the claimed invention “allows for the complete starting volume of a sample to contact each solid support.” This argument is not persuasive for while the sample is required to flow serially through a plurality of supports, there is no requirement that the sample flow through all of the supports, or that all of the sample flow. Rather, all that is required is that at least some of the sample flow through at least two supports. In short, applicant is arguing limitations not in the claims.

As seen above in FIG. 1B and FIG. 2, as well as stated explicitly at column 8, penultimate paragraph, Zanzucchi et al., teaches that a plurality of wells may be connected to each other by means of a common channel. Further, as noted above, Zanzucchi et al., column 11, teaches that a specific binding member may be placed in each of a series of wells. Such teaching speaks directly to flowing the sample through a plurality of wells so to achieve exposing the support to a sample in a serial manner.

Appellant, at page 11 of the Brief, asserts that the claimed invention allows for “rapid collection/separation/elution of different polynucleotides.” And at page 12, first full paragraph, appellant asserts that “[f]urther advantages of various embodiments of this arrangement are discussed in the Application at page 25, line 17 to page 26, line 8.” This argument has not been found persuasive as appellant is again arguing limitations not recited in the claims. Indeed, there

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is no requirement in any of the claims that addresses the speed or rapidity at which the method is to be practiced, much less the speed or rapidity at which any polynucleotide is separated and/or eluted. Furthermore, appellant has neither identified where such a limitation is to be found in the claims nor has submitted evidence showing same. As noted at page 30, "Appendix B Evidence Appendix," of the Brief, "No evidence is being submitted in the present appeal brief."

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Appellant at page 12 of the Brief asserts that "there is no reason to modify the teachings of Zanzucchi to achieve the presently recited elements as presently claimed."

Attention is directed to the decision in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007)

When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

It is further noted that prior art is not limited to the four corners of the documentary prior art being applied. Prior art includes both the specialized understanding of one of ordinary skill in the art, and the common understanding of the layman. It includes "background knowledge possessed by a person having ordinary skill in the art. . . [A] court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR* at 1396.

Suggestion, teaching or motivation does not have to be explicit and “may be found in any number of sources, including common knowledge, the prior art as a whole or the nature of the problem itself” *Pfizer, Inc. v. Apotex, Inc.* 480 F.3d 1348, 82 USPQ2d 1321 (Fed. Cir. 2007) citing *Dystar Textilfarben GMBH v. C. H. Patrick Co.*, 464 F.3d 1356 (Fed. Cir. 2006).

As shown above, Zanzucchi et al., teaches wells in series that allow for the serial passage of a test sample over a specific binding member. Also, Zanzucchi et al., also explicitly teaches that each well may have heating and cooling means as well as means to effect stirring or sample movement. Such explicit teachings speak to combining both serial flow and parallel techniques.

It is noted with particularity that appellant’s traversal of the rejection is predicted on the teachings of Zanzucchi et al., and not on the combined teachings of the cited prior art. While an acknowledgement is made at page 18 that other cited prior art is used, the Brief fails to address the identified teachings and motivation contained therein. Furthermore, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir.1986).

At page 18, bridging to page 19 of the Brief, argument is presented that it would be redundant to have combined Brenner with Okano. It is noted that the rejection is based upon the combined teachings of Zanzucchi et al., Okano et al., and Brenner. As shown above, Zanzucchi et al., teaches incorporating a specific binding partner (an antibody) in a series of wells, yet only teaches using a single nucleic acid probe in a single well. Okano and Brenner each teach using

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multiple probes so to all for the detection/identification of multiple target sequences. Okano also teaches explicitly of subjecting specific probes to a change in a physical property so to effect release of the polynucleotide from the support. In the case of Okano, the support is an array chip, and as such, the different probes may be in a common well. It would have been obvious to the ordinary artisan at the time the invention was made to have modified Zanzucchi et al., by including multiple probes as disclosed by Okano et al., but to have the series of probes in separate wells, as disclosed by Zanzucchi et al., as such would have allowed for the heating/cooling of individual probes and not the entire chip as disclosed by Okano et al.

The ordinary artisan would have also been motivated to have further modified the method of Zanzucchi et al., by including the tag sequences of Brenner as such would have allowed for the identification of a population of sequences, a limitation of claim 24.

Appellant at page 19 of the Brief asserts that the aspect of “simultaneous release of polynucleotides” and the limitation of “where all of the liquid flows through each of the substrates” have not been addressed. Similarly, appellant at page 22 of the Brief, asserts that the prior art does not teach selective heating multiple supports or eluting multiple samples. And at page 22, bridging to page 23 of the Brief, appellant asserts that the aspect of heating multiple supports simultaneously, but rather, teaches a stepwise treatment of wells.

The above argument has not been found persuasive for as shown above, Zanzucchi et al., column 7, penultimate paragraph, teaches that the temperature of the wells can be monitored and changed.

As seen above in FIG. 1B and FIG. 2, as well as stated explicitly at column 8, penultimate paragraph, Zanzucchi et al., teaches that a plurality of wells may be connected to each other by means of a common channel. Further, as noted above, Zanzucchi et al., column 11, teaches that a specific binding member may be placed in each of a series of wells. Such teaching speaks directly to flowing the sample through a plurality of wells so to achieve exposing the support to a sample in a serial manner.

Zanzucchi et al., column 5, teach that the assay device is connected to a computer so that the assay can be conducted and results monitored, and that the computer can also control well-specific heating and cooling means (column 7).

Okano et al., teach that multiple nucleic acid targets (appellant's polynucleotide populations) can be eluted from one or a plurality of fixed capture sequences (probes). At column 3, third paragraph, Okano et al., teach that target polynucleotides are eluted from the chip "via heating and the like." Okano et al., fourth paragraph, teach that the chip comprises a plurality of "wells" in which the probe is immobilized.

In view of such explicit teachings, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified a plurality of wells of Zanzucchi et al., so to allow for the heating and release of target nucleic acids from any number of solid supports found in individual wells as such would be under computer control. By the simultaneous heating of multiple supports, the ordinary artisan would be able to selective elute multiple polynucleotide targets, which is explicitly disclosed by Okano et al. In view of the serial arrangement of the wells and their being connected by a single channel (Zanzucchi et al.) the samples would elute in series, and thereby avoid mixing, a limitation of claim 23.

At page 20 of the Brief argument is presented that the final Office action at page 8, paragraph 26, improperly relied upon appellant's disclosure. For convenience, the cited passage is reproduced below.

26. While the prior art has not been found to suggest specific shapes of the channel, nor the structure of the flow path, such elements are not deemed to rise to the level of a patentable distinction, but rather, constitute obvious design choices. Similarly, the choice of material used to fashion the support is a matter of obvious design choice as they were known in the art and [*sic*, as] no unexpected result is attributable to their use here. In support of this position, attention is directed to page 10, first full paragraph, of the specification, which teaches that the support can be any of the "materials used in standard electrophoresis or chromatographic DNA separation methods." *In re Hopkins* 145 USPQ 140 (CCPA, 1965).

The above argument has not been found persuasive as the statement of applicant has not been relied upon for establishing obvious, but rather, to clarify that the record had not been found to support any potential assertions of secondary considerations of non-obviousness, e.g., the design or shape, or materials of the device used

At page 23 of the Brief, argument is made that the claimed invention requires "the entirety of the mixture flows through each of the solid supports, thereby ensuring that as much of the mixture is screened as possible prior to the mixture passing out of a solid support and into the next solid support. This results in a significant advantage over other possible methods."

The above argument does not identify any element not suggested by the prior art and as such, the advantages are to be expected and do not constitute a patentable distinction. As shown above, Zanzucchi et al., explicitly teaches that one can use the device in a method where the wells are connected by a common channel (column 6, lines 52-54), that the wells can have

individual heating and cooling means (column 7, lines 54-57), and that the specific binding member can be placed into a series of wells so to permit “sequential testing” (column 11, lines 29-31). Zanzucchi et al., also explicitly teaches performing hybridization reactions in the wells (column 10) and Okano et al., at column 3, teaches using multiple nuclei acid probes so to capture multiple target nucleotides, that the probes may be in wells located on the chip, and that specific target nucleotides are released from their probe by heating (column 3).

Clearly, the elements of the claimed assay method, including all dependent claims, were all known in the art at the time of the invention, and that these elements are all performing in a known and predictable manner. Appellant has not shown or demonstrated that any unexpected result is obtained by practicing the claimed invention. As noted above in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007)

When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

Such is the case at hand. For the above reasons, and in the absence of convincing evidence to the contrary, the rejection of claims 21-38 under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,593,838 (Zanzucchi et al.) in view of US Patent 5,607,646 (Okano et al.) and US Patent 5,962,228 (Brenner) should be maintained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner’s answer.

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For the above reasons, it is believed that the rejection should be sustained.

Respectfully submitted,

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TQAS, TC 1600 Appeals Specialist